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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/050,000	05/03/2002	Tiina Nakari-Setala	0365-0529P	4534

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EXAMINER	
AFREMOVA, VERA	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 10/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/050,000	NAKARI-SETALA ET AL.	
	Examiner	Art Unit	
	Vera Afremova	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *10-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of the Group I, claim 1-9, in the reply filed on 8/17/2005 is acknowledged. The traversal is on the ground(s) that correlation between hydrophobins and foam formation has not been know in the prior art and, thus, there is a special technical feature that provides link to all of the present claims. This is not found persuasive because the cited reference by y Nakari-Setala et al. (IDS reference; Eur. J. Biochem. 1997, 248: 415-423) clearly describes that hydrophobins are collected from foam formed in cultivation medium (see page 417, column 2, par. 2, last 5 lines) and, therefore, hydrophobins are foam-associated proteins. The requirement is still deemed proper and is therefore made FINAL.

Claims 10-31 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 8/17/2005.

Claims 1-19 are under examination in the instant office action.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Nakari-Setala et al. (IDS reference; Eur. J. Biochem. 1997, 248: 415-423) disclose cultivating and modifying

microorganism belonging to *Trichoderma reesei* under various culture conditions in a way that the microorganism does not produce one and/or two hydrophobic proteins HFBI and HFB II

Claims are directed to a method for decreasing foam formation during cultivation of microorganisms wherein the method comprises two active steps including step of modifying microorganism in a way that the microorganism does not produce one and/or two hydrophobic proteins and step of cultivating the microorganism. Some claims are further drawn to the microorganisms belonging to *Trichoderma reesei* and to hydrophobic proteins HFBI and HFB II.

The reference by Nakari-Setala et al. teaches that expression of HFBI and HFB II is strongly induced by N and C starvation and by light (entire document including abstract) and that expression of hydrophobins is significantly reduced when microorganism is cultured in the presence of glucose (page 418, column 2, par. 2, last 3 lines). The reference discloses a method for modifying and cultivating microorganism belonging to *Trichoderma reesei* under various culture conditions in a way that the microorganism does not significantly express hydrophobins and thus, it does not significantly produce hydrophobins when cultured in the presence of glucose and/or in the dark (page 416 column 1, par. 4 and par. 7). The cited method comprises both active step as required by the presently claimed invention and, thus, it results in the same effects as the claimed method such as reduction of foam formation during cultivation of microorganism capable to produce hydrophobins. The fact that hydrophobins are associated with foam is acknowledged in the cited reference because the cited reference clearly describes that hydrophobins, when produced, are collected from foam formed in cultivation medium upon bubbling (see page 417, column 2, par. 2, last 5 lines or see page 420, column 2 par. 3).

Thus, the cited reference by Nakari-Setala et al. anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nakari-Setala et al. (IDS reference; Eur. J. Biochem. 1997, 248: 415-423) taken with Wosten et al. ("Interfacial self-assembly of a fungal hydrophobin into a hydrophobic rodlet layer". The Plant Cell, November 1993, Vol. 5, pages 1567-1574) and Spanu et al. ("Deletion of HCF-a, a hydrophobin gene of Cladosporium fulvum, does not affect pathogenicity on tomato". May 1998, Vol. 52, No. 5, pages 323-334).

Claims are directed to a method for decreasing foam formation during cultivation of microorganisms wherein the method comprises step of modifying microorganism in a way that the microorganism does not produce one and/or two hydrophobic proteins and step of cultivating the microorganism. Some claims are further drawn to the microorganisms belonging to *Trichoderma reesei* and to hydrophobic proteins HFBI and HFB II. Some claims are further drawn to genetic modification of microbial genes associated with regulation and production of hydrophobins including deletion of these genes.

The reference by Nakari-Setala et al. discloses that expression of hydrophobins, foam-associated peptides, is strongly induced by source of nutrients and light (entire document including abstract) and that expression of foam-associated hydrophobins, including HFBI and HFB II, is significantly reduced when microorganism *Trichoderma reesei* is cultured in the

presence of nutrients such as glucose. Thus, the reference teaches that the fungal hydrophobin production is modified under suitable culture conditions. The cited reference also suggests modification of hydrophobin production by disruption of genes encoding for hydrophobins (page 421, column 1, par. 2) but the cited reference by Nakari-Setala et al. is lacking actual disclosure about genetic modification of microbial genes associated with regulation and production of hydrophobins.

However, Spanu et al. discloses genetic modification of microbial genes associated with regulation and production of hydrophobins such as deletion of HCF-a, a hydrophobin gene of *Cladosporium fulvum*. Spanu et al. clearly teaches that deletion of hydrophobin gene reduces hydrophobicity of the fungal microorganisms but it does not affect other biological function (entire document including abstract).

The reference by Wosten et al. is relied upon to demonstrate that fungal hydrophobins are assembled on the surface of gas bubbles and they form membrane around air bubbles (see abstract). Thus, hydrophobins are foaming agent during microbial cultivation under aerated conditions by bubbling or in shaken cultures.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to modify microbial hydrophobin production by genetic manipulations with a reasonable expectation of success in reducing foaming during cultivation of the modified microorganisms because hydrophobins are foaming agents and/or foam-associated agents and because prior art teaches and suggests disruption of hydrophobin genes for reduction of hydrophobin production. Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented be the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached at (571) 272-0926.

The fax phone number for the TC 1600 where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology center 1600, telephone number is (571) 272-1600.

Vera Afremova

AU 1651

October 14, 2005

V. Afremova

VERA AFREMOVA

PRIMARY EXAMINER